

## REMARKS

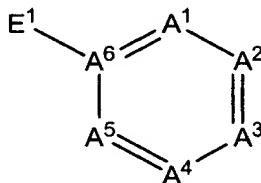
Claims 1-92 are pending. Claims 1-18, 23-29, 34, and 40-92 are withdrawn, and thus claims 19-22, 30-33, and 35-39 are rejected.

Entry of this amendment is proper, because it will clarify the issues on appeal.

Claim 19 is the sole independent claim at issue. It recites a pharmaceutical composition comprising a radiolabeled pharmaceutical agent of the formula (II):

RI-C<sub>h</sub>-L<sub>n</sub>-(BM)<sub>x</sub>; and

an effective stabilizing amount of a compound of formula (I):



The claim defines the components and states "provided the compound of formula (I) is not (1) a substituted monohydroxyl aromatic compound; (2) a substituted dihydroxyl aromatic compound, in which the two hydroxyl groups are not adjacent to each other; (3) a substituted monohydroxyl-monoamino aromatic compound, in which the hydroxyl group and amino group are not adjacent to each other; or (4) an ortho, meta, or para aminobenzoic acid."

## Improper Double Patenting Rejection

The Office Action rejects the claims of the present pending application over claims 22, and 28-30 of U.S. Patent No. 6,537,520 (the '520 patent). The Examiner asserts that the present invention is an obvious variant of the claims, even though no compounds of Formula I are taught or suggested. The Office Action supplies two other references, but as will be

discussed below, a *prima facie* case of obviousness has not been shown, and therefore the rejection is improper.

**No *Prima Facie* Case of Obviousness Established**

The Office Action rejects claims 19-22, 30-33, and 35-39 under 35 USC 103(a) as being obvious over the '520 patent, in view of U.S. Patent No. 5,679,318 (the '318 patent) and the abstract to JP 56144060 to Nippon Oils and Fats Co. (the Nippon reference). The Examiner is respectfully requested to provide an English translation of the full Nippon reference.

The Office Action also rejects claims 19-22, 30-33, and 35-39 under 35 USC 103(a) as being obvious over U.S. Patent No. 5,750,088 (the '088 patent) or U.S. Patent No. 5,707,603 (the '603 patent), in view of the '318 patent and the Nippon reference.

The Examiner has impermissibly boiled the invention down to a gist, namely, that the invention is adding an antioxidant to a radiopharmaceutical. Obviously, those in the art knew the importance of antioxidants. For example, the '520 patent states that its compositions can include a reducing agent. The '520 patent states "Reducing agents useful in the preparation of radiopharmaceuticals and in diagnostic kits useful for the preparation of said radiopharmaceuticals include but are not limited to stannous chloride, stannous fluoride, formamidine sulfonic acid, **ascorbic acid**, cysteine, phosphines, and cuprous or ferrous salts." (col. 34, lines 46-52; emphasis added). Still, the Examiner has not alleged that the listed reducing agents teach or suggest Claim 19's Formula I.

The '088 patent also includes ascorbic acid as a reducing agent. *See* col. 23, lines 30-36. The Examiner has not alleged that the listed reducing agents teach or suggest Claim 19's Formula I.

The Examiner alleges that the '318 patent teaches antioxidants for <sup>90</sup>Y, but again the Examiner has not alleged that any of the antioxidants are included in Claim 19's Formula I.

Thus, a survey of the above radiopharmaceutical-related patents failed to find any antioxidants included in the present application's Formula I of Claim 19.

Nonetheless, the Examiner appears to pick and choose from the abstract of a nonanalogous reference and present a rejection based on a combination of references. As will be seen, the Nippon reference cannot be used to establish a *prima facie* case here.

#### ***The Nippon Reference Is Nonanalogous Art***

Based on the Abstract, the reference relates to an "[a]ntioxidant for feed use," more specifically, the assignee, Nippon Oils & Fats Co., has found a synergistic combination of ascorbic acid and gallic acid (a trihydroxybenzoic acid) which prevents oxidation "of the oil and fat in feed." No disclosure points toward use with radiolabeled pharmaceutical agents. Upon information and belief, the oxidation of fats and oils in feed renders the feed less palatable to cattle, swine, and the like - thus causing reduced consumption and hence, reduced weight gain. Thus, not even a similar problem is solved. Applicants submit that this development is not something that a person of skill in the pharmaceutical art should be imputed to be aware of.

***The Nippon Reference Cannot Be Combined With The Other References***

In response, the Examiner states "An [sic] known antioxidant would have been reasonably expected to function as [sic] antioxidant in any composition." Applicants strongly disagree.

First, the fact that something can be ingested as a feed is hardly evidence that it will function well when parenterally administered as a radiolabeled pharmaceutical agent. Second, not all antioxidants work equally well in pharmaceuticals. For example, the Background section of the '603 patent explains that **choosing the identity of the antioxidant is critical**:

Another problem with some prior art compositions is that the chelator must be activated by a reducing agent before forming the radionuclide chelate. If the protein conjugates are to be formed prior to formation of the radionuclide chelate, then the reducing agent employed for activating the complexing agent can degrade the protein.

Thus, the references of record strongly rebut the implication that antioxidants are interchangeable.

Furthermore, **the Office Action has provided no evidence to support the contention that replacing gentisic acid with gallic acid is "a selection from amongst equally suitable material."** To the contrary, the evidence shows that it is not, or the Office Action would not have had to resort to a reference that is so far afield.

***The Nippon Reference Cannot Be Modified to Meet the Claim Limitations***

Even if the Nippon reference could be relied on, the combination of references fails to teach the claimed invention.

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PATENT  
REPLY FILED UNDER EXPEDITED  
PROCEDURE PURSUANT TO  
37 CFR § 1.116

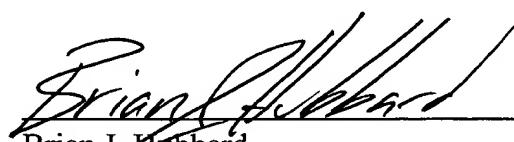
As noted above, the Nippon reference discloses a synergistic combination of ascorbic acid and gallic acid (a trihydroxybenzoic acid) which prevents oxidation "of the oil and fat in feed." We know that it is a synergistic combination, because the Abstract states "the antioxidantising activity of gallic acid is synergically intensified. Oxidn. of the oil and fat in feed, can be prevented."

No teaching of the Nippon reference implies ascorbic acid is optional, in fact, it is necessary to exhibit synergism. Thus, the Nippon reference is limited to combinations including ascorbic acid, because the reference's touting of synergism teaches away from modification in this regard. In contrast, the Applicants do not claim ascorbic acid in their independent claim. Therefore, the claims patentably define over the references.

Thus, taking the references as a whole, the combination of references is improper. Applicants are concerned that the combination of references is due to an impermissible amount of hindsight.

Applicants submit that the claims are in condition for allowance.

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